ABLe 2.2 Test Plan data setup

Before testing ABLe, we must first load a high resolution MRI image into the folder. We will then run the Brain Extraction program in order to create an image which is of the segmented brain. The ABLe program requires both of these images as input.

1. Create a new folder.
2. Using the Open Image dialog box found under the *Image* menu, open the file named $PXHOME/images/MRI-head/head.hdr (where $PXHOME is the MEDx installation directory).
3. To orient the image, Select *Orthogonal* under the *Display* menu. In the Sagittal view, first select the "A" button followed by the "S" button. This will orient the image properly. Select *Verify Orientation*.
4. Under the *FSL* menu in the toolbox, select, *Structural Analysis->BET Brain Extraction*. When the dialog box pops-up, select the *OK* button.
5. The resulting image will need the same orientation step that was applied in (3) above.

We are now ready to test the following functionality of ABLe. The ABLe program can be used to (1) measure volume of a lesion (2) show the percentage of total brain volume taken up by the lesion, (3) register the input brain into Talairach space, (4) report user defined structures in Talairach space, based on VOTL database (5) determine where the lesion intersects Brodmann areas defined by the Damasio Atlas, (6) show the percentage of this intersection, (7) generate an HTML report of results, (8) allow for group lesion analysis as well as a data driven behavioural analysis, (9) display Brodmann area graphics over Damasio slices from the original brain volume, (10) display all or a subset of Brodmann area graphics defined by the VOTL database over the Talairach registered brain .

6. Select the Uturn button at the top of the folder to go back to the brain before being de-skulled.
7. Choose *Display Range* under the *Display* menu. Select *Group/Volume* and then next to Group/Volume, enter 150 for the *Max*, then select *OK*.
8. Under the *Display* menu, choose *Lightbox*. Use the scrollbar to scroll down until slice 36 is at the upper left of the viewer.
9. Select *Outline Lesion & Compute Volume* from the ABLe dialog box (found under the *Volumetric* menu in the toolbox). You will be prompted to outline the lesion in relevant slices on the right hemisphere. On slices 36-38 outline the entire right hemisphere of the brain. This brain does not have a lesion, so we will pretend that the lesion extends across the whole right hemisphere in these three slices. Select *OK*. You will next be prompted to outline the lesion in relevant

slices on the left hemisphere. On slices 36-38 outline the entire left hemisphere of the brain. Select OK to start the volume calculation.

10. A window showing you the lesion volume in units of cc should appear.

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11. You will be prompted to measure the callosal thickness. Select No. This option is available if the researcher wants to measure the corpus collosum in three locations.
12. Select the *Next* button in the ABLe dialog box.
13. Choose the *Select* button and choose "Brain from head.img" as the segmented brain. Then hit the *Select* button.
14. "Brain from head.img" should be written next to *Segmented Brain* and the segmented brain should be visible in the Folder.

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15. Leave all options as default, and select *Register to Template*. Later we will test the options involving registration. For now the only option used was to *Calculate registration accuracy*.
16. A dialog box will ask the user to orient the volume in the orthogonal viewer. It should be oriented correctly, so select *OK*. Registration into Talairach space will take a couple of minutes.
17. When registration is complete, a window should be displayed showing the accuracy of the registration. The value should be approximately 95.42%. In addition the folder shows a fused image of the input brain in color and the Talairach template in gray scale. There should be considerable overlap between the two brains suggestion an accurate registration. Select *No* to the question of specifying a slice range. This would be used if you only wanted the registration accuracy measured over a specific slice range. (Helpful if the MR acquisition from the template does not match the one of the input brain i.e. one includes more brainstem than the other)

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18. A brief message (2 sec) should be displayed, suggesting that the registration process is done.

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19. Select the *Next* button, then choose Generate html Report.
20. In your UNIX terminal window, may a directory called /tmp/able_<your name>. This is where some of the results will be placed.
21. A Patient Demographics window is displayed. Enter 1234 for *Case Number*, Bilateral for *Type of Lesion* and /tmp/able_<your name>/able_<your name> for *Output Directory/Filename.* Select Ok.

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22. A Netscape window appears titled, VOTL Database Search Results. This display contains the patient demographic information, volume loss for both right and left hemisphere, total brain volume, percentage loss of total brain volume, centroid of lesion in Talairach space, registration accuracy, percentage of the lesion in each structure and percentage of each structure taken up by the lesion. For percentage of the lesion in each structure, one can follow the hyperlinks (e.g. Right, Left, or See all) to find specific areas of interest. The VOTL database was provided by Jack Lancaster from the RIC at University of Texas Health Science Center at San Antonio.

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23. You may now exit the Netscape window.
24. Select the *Output for Database* button. Leave the values of Case Number and Type of Lesion as is and select OK. An option to specify the output filename is made available. Instead of /tmp/1234.txt, name the file /tmp/able<your name>/1234_<your name>.txt, then select OK. Using your favorite editor (e.g. vi), make sure that this file was created and has information regarding the percentage of the lesion in each Brodmann area. This file can be loaded into Excel if the user desires.

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25. Select the *Next* button, then select *Save Lesion Volume*. Change the Lesion Image File name to /tmp/able_<your name>/lesion_<your name>.tif and hit the Enter key, then select Save. The image containing just the lesion in Talairach space is now saved. This lesion will be loaded in the next steps to demonstrate the group display aspect of ABLe. No errors should be seen as the lesion image is saved.

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26. The next several steps will test the various group analysis options. Make sure that the *Single Group Analysis* checkbutton is selected. Select the *Load Lesion Volumes* button. Choose the 10 lesion files, p001.tif – p010.tif, previously saved in the $ABLE_TESTDIR directory (/net/medvob/medstor4/ABLe_TestData). This should load the 10 patient lesion images into the folder.

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27. Enter 8 in the *Threshold for # of Subjects* field. If fewer than 8 subject's lesions overlap at any voxel location, then this voxel will not be included in the group lesion report.
28. Select Generate Group html Report. After some seconds, you will be prompted for a report directory and filename. For *Directory/Filename*, enter /tmp/able_<your name>/ablegroup1_<your name>. A Netscape window appears with the Group report. A subheading is labeled Group Analysis with threshold of 8 subjects. In addition, a Colorwash image is created in the folder. This colorwash image represents the group of overlapped lesions overlaid on the template brain image.

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29. You may now exit the Netscape window.
30. Select the *Two Group Analysis* checkbutton. Select the *Load Lesion Volumes* button. Choose the first 5 patient lesion images, p001.tif – p005.tif, for Group A. Make sure you select OK rather than the Apply button in the Open Image dialog box. You will then be prompted to open Group B. Choose the next file patient files, p006.tif – p010.tif and select Open. This should load the first 5 patient images into a group page named *Lesion Group A* and the last 5 patient images into a page named *Lesion Group B.*

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31. Enter 3 for *Threshold # of Subjects A* and 3 for *Threshold for # of Subjects B.* Select Generate Group html Report. After some seconds, you will be prompted for a Group A Only report directory and filename. This Group A report will show where at least 3 subjects have lesion overlap but none in Group B have this overlap. For *Directory/Filename: Group A Only*, enter /tmp/able_<your name>/ablegroupA_<your name>. A Netscape window appears with the Group report. A subheading is labeled Group Analysis: Group A Only. Threshold for number of subjects is 3. You will next be prompted for a Group B Only report directory and filename. For *Directory/Filename: Group B Only*, enter /tmp/able_<your name>ablegroupB_<your name>. A Netscape window appears

with the Group report. A subheading is labeled Group Analysis: Group B Only. Threshold for number of subjects is 3. Finally, you will be prompted for a Group A and B report directory and filename. For *Directory/Filename: Group A and B Only*, enter /tmp/able_<your name>/ablegroupAB_<your name>. A Netscape window appears with the Group report. A subheading is labeled Group Analysis: Group A and B. Thresholds for A and B are 3 and 3, respectively. View the netscape report.

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32. After all reports are completed, a group page containing the three colorwash results will appear in the folder. One by one, select each colorwash image. The first colorwash image represents where at least 3 of the patient's images from Group A share a common lesion area. The second colorwash image represents where at least 3 of the patient's images from Group B share a common lesion area. The third colorwash image represents where at least 3 of the patients from Group A and 3 of the patients from group B overlap.

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33. Select the *Behaviour Analysis* checkbutton. Select the *Load Lesion Volumes* button. Choose all ten patient lesion images, p001.tif – p010.tif and select Open in the Open Image dialog box. This should load all ten lesion images into the folder.

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34. Select the *Behaviour Analysis* button. You will be prompted to enter an input text file name and directory path. Enter $ABLE_TESTDIR/behaviours.txt where $ABLE_TESTDIR is /net/medvob/medstor4/ABLe_TestData. You will also be prompted to enter the minimum number of subjects in the lesion group for a t-test. Enter 3. Select OK.
35. After several minutes of processing, a group page will appear in the folder. This group page contains t-map images (one for each behavior specified in the behaviours.txt file). The pixel value in these t-map images represents the students t value calculated by analyzing the difference from behavioral scores from patients that had lesions as that pixel vs. patients that did not have a lesion at that pixel location. There should be 13 t-map volumes created.

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36. Select the behav_tmap3.img icon. Select Display→Display Range and hit the Compute button. Scroll down to slice 72 and you will see non-zero pixel values representing the t-map values described in step 35. Select the U-turn icon at the top of the folder so that you are viewing the group of 13 t-map volumes.

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37. Select the Decode Subjects button. Enter 3 for the t-map image number. Leave the minimum cluster size at 10 pixels and the minimum t-value at 2. Select OK. A netscape window will display showing the Corrected t-value and degrees of freedom (DOF). In addition, a table appears listing the Talairach x,y,z coordinates of clusters where the t-values in behaviour 3 (B3) are greater than the minimum t-value specified of 2. The t-values for these clusters in all behavior t-maps are displayed in this table. If the t-value is greater than the Corrected t-value it will appear in red. If less than the negative of this t-value it will appear in blue. For this small number of patients, we do not have significant t-values in this table.
38. Exit the netscape window. Go to the Page→Page Manager dialogue. Select the Registered_Tal Image and select Goto Page. Scroll down to slice 90, Select the *Next* button. Select the button labeled *Load Subset of Brodmann Areas from VOTL database*. Choose BA_40 and BA_41 then hit Select. You will see graphics representing these Brodmann Areas overlaid on the image. Now select the button labeled *Load All Brodmann Areas from VOTL database.* You will see graphics representing all Brodmann Areas (derived from the VOTL database) overlaid on the image. Just for informational purposed, these graphics can be overlaid on any image that has been warped into Talairach space.

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39. This completes the first phase of testing. Please close the folder. Please close the ABLe application.
40. We must now re-test the ABLe system by using the D-P Atlas instead of the VOTL database as before. In addition, we will test the option to load a lesion mask instead of tracing the lesion in MEDx. The lesion mask can be generated from outside programs such as MRIcro but must be the same size as the original brain scan and must be 8 bit.
41. Please re-run steps (1) – (8) above.
42. Select *Analysis of Brain Lesions* found under the *Volumetric* option in the toolbox.
43. Select the option labeled *Analyze selected 11 slices from D-P Atlas*.
44. Select *Load Lesion Mask & Compute Volume* from the ABLe dialog box (found under the *Volumetric* menu in the toolbox). When prompted to load your Lesion

Mask, use the Image→Open Image dialogue box to open the $PXHOME/images/tutorials/head_mask.tif file. Then Select OK in the window asking you to load the Lesion Mask to start the volume calculation.

45. A window showing you the lesion volume in units of cc should appear.

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46. Select the *Next* button in the ABLe dialog box.
47. Choose the *Select* button and choose "Brain from head.img" as the segmented brain. Then hit the *Select* button.
48. "Brain from head.img" should be written next to *Segmented Brain* and the segmented brain should be visible in the Folder.

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49. Leave all options as default, and select *Register to Template*. Later we will test the options involving registration. For now the only option used was to *Calculate registration accuracy*.
50. A dialog box will ask the user to orient the volume in the orthogonal viewer. It should be oriented correctly, so select *OK*. Registration into Talairach space will take a couple of minutes.
51. When registration is complete, a window should be displayed showing the accuracy of the registration. The value should be approximately 94.10%. In addition the folder shows a fused image of the input brain in color and the Talairach template in gray scale. There should be considerable overlap between the two brains suggestion an accurate registration. Select *No* to the question of specifying a slice range. This would be used if you only wanted the registration accuracy measured over a specific slice range. (Helpful if the MR acquisition from the template does not match the one of the input brain i.e. one includes more brainstem than the other)

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52. The program will now reslice the input brain according to the Damasion Atlas and extract the 11 Damasio slices.
53. Once complete, a Results window should show the Volume Loss, Percentage Loss and a series of Lesion Intersection Results. It is expected that Brodmann areas 5R, 7R, 18R, 21R, etc will be shown at the bottom of the report. The "R" next to the number represents the right hemisphere. In addition a list of Percentages of BA intersection is displayed at the bottom of the Results viewer.

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54. Select *Dismiss* from the Results viewer.
55. In the folder, a colored image representing the Brodmann areas and a white area representing the lesion should appear.

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56. Select *Next* and then in the *Generate Report* tab of **ABLe**, select *Generate html Report.* For *case number*, enter 1234, for *Type of Lesion*, enter Bilateral, for *Output Directory/Filename*, enter /tmp/able_<your name>/ablereport_<your name>. Then select *OK*.
57. A Netscape browser will pop-up diplaying a report page. This report should contain the Volume Loss, Percentage Loss, Lesion Intersection Results per slice, Percentage of Brodmann Area Intersection and a Lesion Display.

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58. Select *File->Exit* from the Netscape browser.
59. Select *Save Measurements*, and leave the case number and type of lesion as is. When prompted for the filename, enter /tmp/able_<your name>/1234rep_<your name>.txt and select *Save*.
60. In another xterm, type cat /tmp/1234rep_<your name>.txt and make sure that the text file was created. This text file is formatted for Microsoft Excel input.

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61. Select *Talairach Reporting*. Then choose the *Select Voxels* option.
62. The MEDx folder is displaying the input brain after it has been registered to Talairach space. Scroll down until slice 64 is in the upper left corner of the folder. With your mouse, select several pixels on that slice. Note that the Talairach coordinates are reported. The z-axis label should be near –4mm.

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63. Select *OK* in the Script Pause window.
64. Select *Talairach Reporting* again.
65. This time choose *Get full list of structures*. The program has placed the cursor in Marker mode. Select a point on the image in slice 64, then 65 and finally 66. Next, select *OK* in the Script Pause window.
66. ABLe will communicate with the VOTL database (Volume Occupancy Talairach Labels) and display structural results for the three points that you have labeled. Dismiss (exit from) the Netscape results window.

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67. Select the *Next* button and you will be placed in the *Lesion Manipulation* section.
68. Select *Save Lesion Volume*. A default file name called */tmp/.able/lesion.tif* is chosen. You may leave this as the filename and then select *Save*. An image representing the lesion on the 11 Damasio slices has been saved to disk.
69. Now select *Load Lesion Volumes*. The default should be */tmp/.able/lesion.tif*. Select *Load* and the lesion image should be loaded into the MEDx folder. This will be a binary image which appears nearly as a series of horizontal lines

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70. So that we can overlay more than one lesion, repeat step 69.
71. Select *Display Group of Lesions*. As the Script Update suggests, first select the page labeled *Lesion* and then the page labeled *Lesion.1* and then hit *Select*. An image showing the outline of Brodmann areas on the Damasio slices will appear as well as gray level pixels representing the lesion. Using the pixel reporter, note that the lesion pixels have a value of 2. This means that two lesions are overlapping at this pixel coordinate. If three pixels were overlapping here the intensity value would be three.

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72. Select *Generate Group html Report*. For the *Descriptive Title* enter *Same Lesion twice*. For *Number of Lesions*, enter *2*. Note that you must have more than one lesion for this report. Enter /tmp/able_<your name>/ablereport_jeff as the *Output Directory /Filename*. Select OK. A Netscape report will be displayed showing the results. The header of the report should contain the descriptive text and number of lesions. A table is then displayed showing how many voxels overlap. There should be no overlap in 0 lesion voxels. 2 Subjects should show some overlap. Finally, the eleven Damasio Atlas slices are displayed with the overlapping lesions. Each image is a separate gif file.

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73. Exit from Netscape.
74. Select the *Next* button. You should now be in the *Display Brodmann Regions* notebook tab. Select *Load Brodmann Atlas*.
75. The eleven Damasio Atlas slices from the lesioned image are displayed with all of the Brodmann area graphics overlaid. These graphics were drawn by a neuroradiologist to match the Damasio Atlas.

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76. Select slice 5 and zoom up once.
77. Make sure your cursor is not in pixel reporter mode and then select one of the graphics. The graphic should now have a yellow bounding box. Select the *Get Brodmann # From Graphic* button.
78. A window should display this particular Brodmann area. The number is the Brodmann area and the letter represents left (L) or right (R).

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79. Select *OK* in the *Script Pause* window.
80. Select *Cancel* from the ABLe dialog box. We are not quite finished however. We will next test the registration options.
81. Close the current folder and then repeat steps (1) – (11).

82. Select the option labeled *Landmark-based Talairach Registration*. This option overrides the automated registration operation and replaces it with a manual placement into Talairach space based on 8 landmark postions. After making this selection, the Segmented Image selection should be replaced with the following text: "*Selecting manual registration causes the automated registration options below (shown in red) to be unavailable*." Now select *Register to Template*. When prompted to orient the volume, select Verify Orientation, then Select *OK* in the Script Pause window. Control graphics should appear on the image and the Talairach Atlas Registration dialog box should be visible.

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83. Place the anatomic labels on the control graphics to their proper positions. You may need to consult the tutorial on Talairach Atlas registration to complete this step. Once the landmarks have been placed, select OK in the Talairach Atlas Registration dialog box. Finally, select OK in the Script Pause window. The registration will be performed and a brief message suggesting that Registration is complete will be presented. The brain is now in Talairach space and has Talairach coordinates.

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This concludes our analysis of Analysis of Brain Lesions.